

Systemic and systemicplus regional antibiotic prophylaxis with cefazolin in total knee arthroplasty: A comparative study

Regional antibiotic prophylaxis in TKA

Recep Öztürk¹, Alieker Yapar¹, Emin Kürşat Bulut¹, Galip Beltir¹, Emre Özanel², Bedii Şafak Güngör¹

¹Department of Orthopedics and Traumatology, Dr Abdurrahman Yurtaslan Ankara Oncology Training and Research Hospital

²Department of Orthopaedics and Traumatology, Kahramanmaraş Necip Fazıl City Hospital, Ankara, Turkey

Abstract

Aim: Different studies show that prophylactic antibiotic concentration is higher with regional application compared to systemic application in total knee arthroplasty surgeries. The results of cefazolin, one of the most commonly used prophylactic agents, are not clear between systemic and local application after tourniquet.

Material and Methods: Forty-three patients with systemic intravenous (iv) 1000 mg cefazolin applied one hour before TKA surgery were compared with 29 patients who were treated with 1000 gr of cefazolin in the foot vein after tourniquet application in addition to the application of cefazolin 1000 g iv, all patients were evaluated in terms of infection findings on the 30th and 90th postoperative days. All patients were followed for at least 2 years.

Results: None of the patients had side effects after cefazolin application during or after surgery. There were no infections of the surgical site in the early postoperative period or during the follow-up period (mean duration, 41,5 months). In Group 1, only one patient had a superficial infection requiring drainage and antibiotherapy. Four patients in Group 1 and one patient in Group 2 had superficial infection treated with only antibiotherapy, respectively.

Discussion: Regional prophylaxis seems to be safe and valuable in TKA. Local plus systemic prophylactic antibiotics were more effective than intravenous administration of the same dose in TKA.

Keywords

Local prophylaxis; Cefazolin; Knee arthroplasty; Infection; Prophylaxis

DOI: 10.4328/ACAM.20330 Received: 2020-09-01 Accepted: 2020-11-26 Published Online: 2020-12-09 Printed: 2021-05-15 Ann Clin Anal Med 2021;12(Suppl 1): 558-62

Corresponding Author: Recep Öztürk, Dr Abdurrahman Yurtaslan Ankara Oncology Training and Research Hospital, Vatan Street, 06200 Yenimahalle, Ankara, Turkey.

E-mail: ozturk_recep@windowslive.com P: +90 5054634794 F: +903123360909

Corresponding Author ORCID ID: <https://orcid.org/0000-0002-6753-9321>

Introduction

Infection rates after total knee arthroplasties (TKA) are higher than after total hip arthroplasty, and infection rates have been reported from 1% to 5% [1]. Although a small number of patients have deep infection, they may be destructive and result in significant morbidity, which often requires additional surgery and long-term antibiotic therapy [2]. Therefore, antimicrobial drugs are generally used for prophylaxis [3].

Gram positive cocci are the most common pathogens in infected orthopaedic prostheses, and staphylococci constitute 75% of infections [4].

The most commonly used antibiotics are cephalosporins and semi-synthetic penicillins in the TKAs [5]. By many authors, routine prophylaxis is applied as multiple cefazolin doses in clean surgical procedures, including elective orthopaedic surgeries [6,7]. Most of the early post-operative infections are the result of intraoperative contamination of the surgical site [8]. In order for antibiotic prophylaxis to be effective, the concentration of antibiotics in the tissues must exceed the minimum inhibitory concentration (MIC) of the infectious organisms during the period between skin incision and wound closure. Coagulase negative staphylococci (CoNS) have relatively high MICs against cephalosporins. Therefore, the conventional systemic prophylactic dose of cephalosporin may lead to insufficient concentrations of these organisms in the tissues [9-11].

The application of a regional drug using a tourniquet allows the drug to achieve higher tissue concentrations than systemic application by providing the targeted limb distribution. Some authors have used a foot vein cannula to administer prophylactic antibiotics in TKA. With this approach, significantly higher concentrations of antibiotics in the tissues at the surgical site can be achieved without systemic side effects [1,12-14].

In the literature, there are studies of the regional antibiotic application with the aid of a foot vein or intraosseous application in TKA (Table 1). These studies are mostly aimed at finding drug penetration into tissues. We have not found any study including comparative clinical results between systemic and systemic+regional cefazolin in the literature [1, 10-18].

In this retrospective study, we planned to define the efficacy and safety of systemic and regional prophylaxis with cefazolin in monolateral TKA. The aim of this study is to evaluate the comparative clinical outcomes after regional antibiotherapy.

Material and Methods

Seventy-two consecutive patients of both gender who admitted to our orthopaedics clinic between January 2014 and December 2016 and underwent elective monolateral total knee arthroplasty for chronic degenerative joint disease were included in this study. The mean age was 67.7±7 std (52-84 years) (9 males and 63 females) (Table 2). Exclusion criteria were penicillin allergy, local or systemic active infection and previous operation history on the same knee. Data collection permissions were obtained from all patients to see the effects of local and systemic prophylactic application of cefazolin. The local medical expertise and education board approved the study protocol.

In the first group, 43 patients, 1000 mg of cefazolin was dissolved in 3ml of 0.9% sodium chloride solution and

intravenously applied from the forearm veins one hour before the operation. In these patients, the tourniquet was inflated to 400 mm Hg (approximately 50 kPa) after 1 hour of cefazolin application. In the second group of 29 patients, in addition to intravenous cefazolin, after tourniquet 400 mm Hg (ca. 50 kPa) inflation, 1000 mg of cefazolin, which is dissolved in 3ml of 0.9% sodium chloride solution was administered to the foot veins intravenously with bolus injection as a regional prophylaxis.

In both groups, the tourniquet was released after surgery and then hemostasis was performed. Jones bandage was applied to all patients. All patients in both groups received 1000 mg of cefazolin intravenously at the sixth hour after the operation. None of the patients used additional oral or parenteral antibiotics. All patients were evaluated for infection findings on the post-operative 30th and 90th days. All patients were followed for at least 2 years.

All operations were performed by the same three surgeons in the same operating room (with laminar flow). The skin on the surgical site was shaved with a disposable razor.

Briefly, a primary operative incision and/or implanted prosthesis infection or infections in the adjacent bone was considered a prophylactic failure. Also, any drainage procedure or debridement of surgical site and prosthesis was considered prophylaxis failure.

At least a two-year follow-up period was planned for all patients. The patients were clinically checked 15 days after discharge and at 1st, 3rd, 6th, and 12th months postoperatively. Then they were called at intervals of 1 year and were clinically examined when necessary.

Statistical analysis

Statistical analysis was performed using the SPSS 22.0 (Chicago IL) computer program; in statistical analysis, categorical variables were given as numbers and percentages, and continuous variables were presented with mean±standard deviation (SD) and median (min-max value) for descriptive analyses. The sample calculation was performed with the Gpower 3.1 program. The effect size calculated in the light of the data of the reference study [19] was calculated as 0.4. The number of samples was calculated between 80% power and 95% confidence interval and found to be 69. The minimum number of patients required to participate in this study was 69 and 76 patients were enrolled in this study. Chi-Square tests were used for comparison of categorical variables between groups. The conformity of continuous variables to the normal distribution was evaluated using visual (histogram and probability graphs) and analytical methods (Kolmogorov-Smirnov/Shapiro-Wilk tests). The Mann-Whitney U test was used for comparison of datasets which were not normally distributed for the variables. An Independent Sample test was used for comparison of datasets, which were normally distributed for the variables. $P < 0.05$ was considered statistically significant.

Results

In the study period, monolateral TKR was applied to 72 patients. Systemic antibiotic prophylaxis was applied to 43 patients and systemic+local antibiotic prophylaxis was applied to 29 patients.

Table 1. Articles investigating regional administration of prophylactic antibiotics in TKA.

Authors	Comparison	Outcomes
Hoddinott et al. [12]	100 mg IV cefomandol application was compared with 750 mg regional sefuroxim application to the foot vein.	The mean cefuroxime was higher in the bone (130 mg / L) and fat (88 mg / L) than cefomandole (9 mg / L and 10 mg / L, respectively); p<0.001
De lalla et al. [3]	Penetration study, 24 patients, compared 800 mg IV teicoplanin and 400 mg teicoplanin application to the foot vein	Overall, the mean concentrations obtained by regional route prophylaxis were 2 to 10 times higher than those obtained by systemic route; p <0.05
De lalla et al. [4]	Clinical study, THA was applied to 205 knees of 160 patients, teicoplanin was applied to the foot vein.	At least 2 years of follow-up, no deep infection, 1 superficial infection was seen.
Lazzarini [13]	Penetration study, 800 mg IV application of teicoplanin and 200 mg foot vein were compared.	When regional prophylaxis is applied, teicoplanin concentrations were approximately 2-times higher.
Young et al. [23]	22 patients, 1 g IV and 1 g intraosseous cefamezin were compared.	In the intraosseous group fat 186 / g, bone 130 ousg / g; In the systemic group oil 11 veg / g and bone 130 tag / g.
Young et al. [22]	30 patients, 250 - 500 mg vancomisin IORA and vancomisin application of 1000 mg vancomycin were compared.	In the 250-mg IORA, 14 lg / g fat, 16 lg / g bone, 44 mg / g fat in the 500-mg IORA group, 38 lg / g bone, 3.2 lg / g fat in the IV group and 4.0 lg / g bone.
Chin et al. [1]	22 patients, 15 mg / kg IV vancomycin and 500 mg IORA were compared.	In IORA fat 39.3 mg / g, bone 34.4 mg / g and in group IV 4.4 mg / g fat and 6.1 mg / g bone (P < .01).
Young et al. [21]	6 groups, a mouse model, control group, systemic cefazolin, IORA of cefazolin, systemic vancomycin, low-dose systemic vancomycin, and low-dose IORA of vancomycin	In prophylaxis with cefazolin and vancomycin, IORA is more effective than IV administration, p = 0.0183
Young et al. [24]	Ten patients with 1000 mg IV vancomycin and 10 patients with 500 mg intraosseous vancomycin were compared (in revision knee prosthesis).	The mean vancomycin was higher in the intraosseous group fat (3.7 mg/g), bone (6.4 mg/g), than the IV group fat (49.3 mg / g) bone(77.1 mg / g); p < 0.001

Table 2. Baseline characteristics

Parameters (n=72)	
Age, years	
Mean±sd	67,7±7,5
Median(min-max)	68,0(52,0-84,0)
Sex, n(%)	
Male	9(12,5)
Female	63(87,5)
Follow-up Time	
Mean±sd	41,5±10,5
Median(min-max)	41,5(24,0-59,0)
Prophylaxis, n(%)	
Yes	29(40,3)
No	43(59,7)
Infection, n(%)	
Yes	6(8,3)
No	66(91,7)
sd: standart deviation	

Table 3. Evaluation of patients according to Prophylaxis

N=28	Prophylaxis		P
	Yes (n=29)	No (n=43)	
Age, years			
Mean±sd	68,0±8,4	67,5±7,0	0,7851
Median(min-max)	68,0(53,0-84,0)	68,0(52,0-84,0)	
Sex, n(%)			
Male	5(17,2)	4(9,3)	0,4702
Female	24(82,8)	39(90,7)	
Follow-up Time			
Mean±sd	44,4±11,8	39,5±9,1	0,0523
Median(min-max)	48,0(24,0-59,0)	39,0(24,0-57,0)	
Infection, n(%)			
Yes	1(3,4)	5(11,6)	0,3912
No	28(96,6)	38(88,4)	

sd: standart deviation
 1. Independent Sample Test
 2. Chi-Square Test
 3. Mann-Whitney U test

All 72 patients were evaluated for both efficacy and safety of cefazolin prophylaxis.

No statistically significant difference was found among age, sex distribution and follow-up period between the groups (Table3). None of the patients had any side effects during or after surgical cefazolin application.

In the follow-up period of two years or more, superficial infection was observed in 8.3% of the patients in the postoperative period (Table2) (p>0,05). Both groups had no deep prosthesis infection requiring additional surgical intervention. Type 1 [4] superficial infection, which can be completely treated with antibiotherapy, occurred in 4 patients in the group without additional prophylaxis and in 1 patient in the group with additional prophylaxis of this infection. Also, one patient in the patient group without additional prophylaxis, a 62-year-old female patient, developed type 2b 4 superficial infections requiring surgical drainage and antibiotherapy. There was no specific risk factor in this patient for infection (advanced age, obesity, diabetes mellitus, etc.). On the 10th post-operative day, she was admitted with the complaint of knee pain and purulent discharge in the surgical incision. On physical examination, the patient had a fever of 38.5°C. C-reactive protein level was high and leukocytosis was present in her laboratory tests results.

The rate of infection was 3.4% in the local+systemic prophylaxis group and 11.6% in the systemic prophylaxis group. There was no statistically significant difference between the two groups in the frequency of infection (p=0.391) (Table3).

Surgical drainage and systemic antibiotic therapy (given for 2 week) were successfully performed, and this resulted patient's recovery without morbidity. No bone or implant infection occurred during the next 3.5 years of follow-up.

The mean follow-up period was 41,5 months (between 24 and 59 months). When the groups were evaluated separately, the mean follow-up period in the first group was 39,7 month, and the mean follow-up time was 42,5 month in the second group. Any deep prosthesis infection requiring removal of the implant and replacement with another prosthesis was not observed in any patient in the long-term follow-up period (2 to 5 years).

Discussion

Prosthetic joint infection (PJI) is one of the most serious complications affecting a patient's quality of life after arthroplasty. The incidence of PJI for primary hip and knee arthroplasties in the literature is 1 % and 2 %, respectively [20]. The incidence of PJI after TKA surgery, according to Turkish National Surveillance Report in 2013, is 0,7-1,7 by (<http://www.saglik.gov.tr/DH/dosya/1-88693/h/uhesa-analiz-2013.pdf>).

Therefore, prevention of post-operative infection is extremely important in this surgical discipline, and antibiotic prophylaxis is applied as routine in TKA. The benefits of prophylactic antibiotics were confirmed by a meta-analysis published in 1997 comparing this anti-microbial administration with placebo or no prophylaxis [2].

PJIs can be classified as acute (first 3 months after surgery), delayed (3 to 24 months after surgery) or late (24 months or more after surgery) [21]. Early and delayed infections are thought to be caused by organisms that occur during surgery, whereas late infections are more likely to be acquired as hematogenous. In addition, according to the classification system (proposed by Gorbach et al. in 1992), infections can be grouped as superficial wound infection or suture abscess (class I), subcutaneous infection requiring antibiotics (class IIa), subcutaneous infection requiring antibiotics and surgical debridement or drainage (class IIb), and prosthesis and/or adjacent bone infection shown in surgery or autopsy (class III) [4].

In recent years, studies have reported that resistance to cephalosporins is significantly increased in coagulase-negative streptococci. However, this increase in resistance is consistent with clinical data on coagulase-negative streptococci. Regional administration of antibiotics can provide better protection against CoNS by achieving higher tissue concentrations [9, 10, 22]. Regional method of delivery would provide lower doses in a more rapid fashion to decrease the risk of toxicity while still seeking to maintain adequate tissue perfusion [23].

Although some antibiotics such as aminoglycosides and fluoroquinolones exhibit concentration-dependent killing, for β -lactam antibiotics such as cefazolin, time above MIC is the most important factor. However, higher β -lactam concentrations are known to lead to an earlier initiation of bacterial killing, which may be more important for prophylaxis against infection when the goal is to prevent initial bacterial adherence and colonization [24].

TKA surgery requires the use of a tourniquet completely obstructing systemic circulation to achieve a bloodless surgical treatment. In most cases, this tourniquet is left in place during the surgery, thus preventing penetration of antibiotic into the leg tissues through the arterial blood flow [13]. As a result, the obtained antibiotic bone levels may be lower than those obtained from other localizations during TKA. Researchers are trying different ways to eliminate this problem with prophylactic antibiotics.

Local prophylaxis practices include local irrigation with antibiotics, foot vein and intraosseous applications [1, 10, 13-18]. Potential complications of intraosseous infusions include fluid extravasation with compartment syndrome due to improper

needle placement in emergencies. Needle site infection has rarely been reported, and it is associated with the time needle is left in intraosseous way. Sub-clinical fat embolism has been observed histologically in animal studies [25].

Currently, the most common drugs used in prophylaxis of TKA are cephalosporins such as cephazoline, cefuroxime and cephalodol [14]. We aimed to evaluate the clinical outcomes of regional prophylaxis with cefazolin by foot vein cannulation.

In 1990, Hoddinott et al. compared a regional cephalosporin (cefuroxim) given 1g into a foot vein with 1g of systemic cefamandole in five patients who underwent routine total knee arthroplasty, and they found that when applied regionally, the tissue concentration was 5-30 times higher. They found this method to be effective in maintaining high concentrations of cefuroxime in the surgical tissues [13]. In 1993, Lalla et al. found that teicoplanin levels after local administration of 400 mg teicoplanin to a foot vein were 2-10 times higher than levels obtained after 800 mg intravenous systemic prophylaxis in the tissues of the surgical site [12].

In 2000, Lalla et al. published the good clinical results of the application of teicoplanin into a foot vein in a patient who underwent 205 knee arthroplasty [1]. Lazzarini et al., in their tissue penetration study in 2003, found that teicoplanin injected into a vein of the foot was about twice as high as systemic [14]. Young et al. published the results of intraosseous application with cefamezin and vancomycin in 2013 and 2014. In both studies, tissue concentrations were higher than intravenous application [10,17].

In 2015, Chin et al. found the superiority of intraosseous application with vancomycin over intravenous application [15]. In 2015, Young et al., who continued their studies on this subject, found that intraosseous application with cefamezin or vancomycin had better results in the mouse model study compared to the control group. Finally, in 2018, Young et al. found high tissue concentrations in intraosseous vancomycin application in patients undergoing revision knee arthroplasty [7,16].

Our study and this literature review show that regional prophylaxis application is the preferred way used for prophylaxis regardless of the drug in TKA. Each antibiotic is potentially suitable for this route. However, the drug is rapidly released into the systemic circulation when the tourniquet is extinguished. Therefore, antibiotics suitable for regional prophylaxis are those that can only be applied as an intravenous bolus injection. Our study has some limitations. Our study is a retrospective analysis and the population is relatively small. The benefit of the new method in our study could not demonstrate statistical significance, but the rate of infection was lower in the new method. Further studies with a larger number of patients are needed in the future.

Conclusion

The regional route for prophylaxis in total knee prostheses is one of the best routes clinically and analytically regardless of which drug is used. A local antibiotic can be applied via a foot vein after the tourniquet is inflated. Local administration of cefazolin, in addition to intravenous prophylaxis, is a reliable and feasible prophylaxis technique in primary elective total knee prosthesis.

Acknowledgment

The authors would like to thank investigators, patients and their families.

Scientific Responsibility Statement

The authors declare that they are responsible for the article's scientific content including study design, data collection, analysis and interpretation, writing, some of the main line, or all of the preparation and scientific review of the contents and approval of the final version of the article.

Animal and human rights statement

All procedures performed in this study were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards. No animal or human studies were carried out by the authors for this article.

Funding: None

Conflict of interest

None of the authors received any type of financial support that could be considered potential conflict of interest regarding the manuscript or its submission.

References

- de Lalla F, Viola R, Pellizzer G, Lazzarini L, Tramarin A, Fabris P. Regional prophylaxis with teicoplanin in monolateral or bilateral total knee replacement: an open study. *Antimicrob Agents Chemother.* 2000;44(2):316-19.
- Gillespie WJ. Prevention and management of infection after total joint replacement. *Clin Infect Dis.* 1997;25(6):1310-7.
- Paya CV, Wilson WR, Fitzgerald RH. Management of infection in total knee replacement. *Curr Clin Top Infect Dis.* 1988; 9:222-40.
- Gorbach SL, Condon RE, Conte JE Jr, Kaiser AB, Ledger WJ, Nichols RL. Evaluation of new anti-infective drugs for surgical prophylaxis. *Infectious Diseases Society of America and the Food and Drug Administration. Clin Infect Dis.* 1992;15(Suppl 1.):S313-38.
- Nichols RL, Condon RE, Barie PS. Antibiotic prophylaxis in surgery--2005 and beyond. *Surg Infect (Larchmt).* 2005;6(3):349-61.
- Evrard J1, Doyon F, Acar JF, Salord JC, Mazas F, Flamant R. Two-day cefamandole versus five-day cephazolin prophylaxis in 965 total hip replacements. Report of a multicentre double blind randomised trial. *Int Orthop.* 1988;12:69-73.
- Nelson JP, Fitzgerald RH Jr, Jaspers MT, Little JW. Prophylactic antimicrobial coverage in arthroplasty patients. *J Bone Joint Surg Am.* 1990;72(1):1.
- Fletcher N, Sofianos D, Berkes MB, Obremskey WT. Prevention of perioperative infection. *J Bone Joint Surg Am.* 2007;89(7):1605-18.
- Yamada K, Matsumoto K, Tokimura F, Okazaki H, Tanaka S. Are bone and serum cefazolin concentrations adequate for antimicrobial prophylaxis? *Clin Orthop Relat Res.* 2011;469(12):3486-94.
- Young SW, Zhang M, Freeman JT, Vince KG, Coleman B. Higher cefazolin concentrations with intraosseous regional prophylaxis in TKA. *Clin Orthop Relat Res.* 2013;471(1):244-9.
- Zalavras CG. Regional Intraosseous Administration of Prophylactic Antibiotics is More Effective Than Systemic Administration in a Mouse Model of TKA. *Clin Orthop Relat Res.* 2015; 473(11): 3585-7.
- de Lalla F, Novelli A, Pellizzer G, Milocchi F, Viola R, Rigon A, et al. Regional and systemic prophylaxis with teicoplanin in monolateral and bilateral total knee replacement procedures: study of pharmacokinetics and tissue penetration. *Antimicrob Agents Chemother.* 1993;37:2693-8.
- Hoddinott C, Lovering AM, Fernando HC, Dixon JH, Reeves DS. Determination of bone and fat concentrations following systemic cefamandole and regional cefuroxime administration in patients undergoing knee arthroplasty. *J Antimicrob Chemother.* 1990;26:823-9.
- Lazzarini L, Novelli A, Marzano N, Timillero L, Fallani S, Viola R, et al. Regional and systemic prophylaxis with teicoplanin in total knee arthroplasty: a tissue penetration study. *J Arthroplasty.* 2003;18:342-6.
- Chin SJ, Moore GA, Zhang M, Clarke HD, Spangehl MJ, Young SW. The AAHKS Clinical Research Award: Intraosseous Regional Prophylaxis Provides Higher Tissue Concentrations in High BMI Patients in Total Knee Arthroplasty: A Randomized Trial. *J Arthroplasty.* 2018;33(Suppl. 7):S13-18.
- Young SW, Roberts T, Johnson S, Dalton JP, Coleman B, Wiles S. Regional Intraosseous Administration of Prophylactic Antibiotics is More Effective Than Systemic Administration in a Mouse Model of TKA. *Clin Orthop Relat Res.* 2015;473:3573-84.
- Young SW, Zhang M, Freeman JT, Mutu-Grigg J, Pavlou P, Moore GA. The Mark Coventry Award: Higher tissue concentrations of vancomycin with low-dose intraosseous regional versus systemic prophylaxis in TKA: a randomized trial. *Clin Orthop Relat Res.* 2014;472:57-65.
- Young SW, Zhang M, Moore GA, Pitto RP, Clarke HD, Spangehl MJ. The John N. Insall Award: Higher Tissue Concentrations of Vancomycin Achieved With Intraosseous Regional Prophylaxis in Revision TKA: A Randomized Controlled Trial. *Clin Orthop Relat Res.* 2018;476(1):66-74.
- Alp E, Cevahir F, Ersoy S, Guney A. Incidence and economic burden of prosthetic joint infections in a university hospital: A report from a middle-income

country. *J Infect Public Health.* 2016;9(4): 494-8.

- Gallo J, Kolar M, Novotny R, Rihakova P, Ticha V. Patho-genesis of prosthesis-related infection. *Biomed Papers.* 2003;147:27-5.
- Zimmerli W, Trampuz A, Ochsner PE. Prosthetic-joint infections. *N Engl J Med.* 2004;351(16):1645-54.
- Nickinson R, Board T, Gambhir A, Porter M, Kay P. The microbiology of the infected knee arthroplasty. *Int Orthop.* 2010; 34(4):505-10.
- Dietz MJ. CORR Insights®: The John N. Insall Award: Higher Tissue Concentrations of Vancomycin Achieved With Intraosseous Regional Prophylaxis in Revision TKA: A Randomized Controlled Trial. *Clin Orthop Relat Res.* 2018;476(1):75-6
- Craig WA. Pharmacokinetic/pharmacodynamic parameters: rationale for antibacterial dosing of mice and men. *Clin Infect Dis.* 1998;26(1):1-10.
- Hasan M, Kissoon N, Khan T, Saldajeno V, Goldstein J, Murphy S. Intraosseous infusion and pulmonary fat embolism. *Pediatr Crit Care Med.* 2001;2(2):133-8.

How to cite this article:

Recep Öztürk, Alekber Yapar, Emin Kürşat Bulut, Galip Beltir, Emre Öznelağan, Bedii Şafak Güngör. Systemic and systemicplus regional antibiotic prophylaxis with cefazolin in total knee arthroplasty: A comparative study. *Ann Clin Anal Med* 2021;12(Suppl 1): S58-62